Reply

We applaud Drs. Opotowsky and Landzberg for having resurrected the interesting paper of William Osler, whose great perception led him to anticipate what we have proved more than a century later, namely, that bicuspid aortic valves (BAVs) with fusion of right and left leaflets and BAVs with fused right and noncoronary leaflets are different etiological entities. Unfortunately, we did not refer to Osler's publication when reviewing the literature to organize our paper. Otherwise, we would have included a comment on this subject in our paper. Moreover, we particularly appreciate the remarks of our colleagues in Boston because they show how important it is to keep in mind classic work, of which a plethora of consistent, although very often overlooked, notions continue to stay alive.

We also applaud the comments of our colleagues on the papers of Tzemos et al. (2) and Biner et al. (3). We agree that including the BAV morphotype as a variable in these studies would probably extend their conclusions. Moreover, we encourage the authors of the many research papers on the pathophysiology, association, and genetics of the BAV to perform, when possible, retrospective studies distinguishing between the BAV morphotypes of their probands. When this distinction has been made, important conclusions have resulted, such as the fact that the BAV morphotype is able to predict the elastic properties of the ascending aorta (1) and the velocity of progression of the aortic dilation (4). We are confident that the new findings on the etiology of BAV disease will draw out new and revealing knowledge in this field in the coming years.

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REFERENCES

1. Schaefer BM, Lewin MB, Stout KK, et al. Usefulness of bicuspid aortic valve phenotype to predict elastic properties of the ascending aorta. Am J Cardiol 2007;99:686–90.
2. Tzemos N, Lyseggen E, Silversides C, et al. Endothelial function, carotid-femoral stiffness, and plasma matrix metalloproteinase-2 in men with bicuspid aortic valve and dilated aorta. J Am Coll Cardiol 2010;55:660–8.
3. Biner S, Rafique AM, et al. Aortopathy is prevalent in relatives of bicuspid aortic valve patients. J Am Coll Cardiol 2009;53:2288–95.
4. Thanassoulis G, Yip JW, Filion K, et al. Retrospective study to identify predictors of the presence and rapid progression of aortic dilatation in patients with bicuspid aortic valves. Nat Clin Pract Cardiovasc Med 2008;5:821–8.

Cardiac Rehabilitation, Exercise Training, and Anxiety

We read with great interest the large study from the young Swedish cohort (1) and the meta-analysis of 20 studies involving nearly 250,000 persons (2), as well as the insightful editorial by Dr. Dimsdale (3) demonstrating the importance of anxiety as a risk factor for major coronary heart disease (CHD) events and cardiovascular (CV) mortality. Although the editorial mentions the possibility of treatments aimed at alleviating anxiety (e.g., medications, psychotherapy, stress reduction, lifestyle alteration) (3), none of these papers mentioned the readily available proven treatment with exercise training.

Nearly 1 decade ago, in a study of 500 CHD patients, we reported a prevalence of anxiety and very high anxiety of 27% and 13%, respectively, with reductions in the prevalence by 56% and 69%, respectively, after formal cardiac rehabilitation and exercise training (CRET) programs (4). More recently, we demonstrated a very high prevalence of anxiety of 28% among 104 younger CHD patients (age <55 years, mean 48 ± 6 years) compared with only 14% ($p < 0.01$) among 260 older patients (age >70 years, mean 75 ± 3 years), with a 69% reduction in the prevalence for the younger patients ($p < 0.001$) and a 32% reduction for the older patients ($p < 0.01$) after formal CRET (5). Moreover, we also recently demonstrated that elevated psychosocial stress (a marker of depression, hostility, and/or anxiety) strongly predicted a higher 3-year mortality after major CHD events, with nearly all of the excess mortality confined to patients with high psychosocial stress who did not significantly improve their level of cardiorespiratory fitness with CRET (6). Patients without psychosocial stress, as well as patients with elevated psychosocial stress who significantly improved their fitness, had very low mortality during follow-up. Although our data are specifically from patients with CHD after major CHD events, we believe that these data can also be extrapolated to primary prevention. In fact, a recent meta-analysis, mostly from non-CV disease cohorts, demonstrates that exercise training significantly reduces anxiety symptoms (7).

Although these data have been emphasized to the lay public (8), we are concerned that the benefits of exercise training on emotional behaviors, and specifically anxiety, have not been emphasized to physicians, including specialists in CV diseases. We agree with these *Journal* papers (1–3) that anxiety is an important and often overlooked risk factor for CV diseases. Certainly, this information provides an additional reason to routinely refer for, and strongly recommend CRET programs to, patients after major CHD events (9).

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